Canadian guidelines for acute bacterial rhinosinusitis

Clinical summary

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Abstract

Objective To provide a clinical summary of the Canadian clinical practice guidelines for acute bacterial rhinosinusitis (ABRS) that includes relevant considerations for family physicians.

Quality of evidence Guideline authors performed a systematic literature search and drafted recommendations. Recommendations received both strength of evidence and strength of recommendation ratings. Input from external content experts was sought, as was endorsement from Canadian medical societies (Association of Medical Microbiology and Infectious Disease Canada, Canadian Society of Allergy and Clinical Immunology, Canadian Society of Otolaryngology—Head and Neck Surgery, Canadian Association of Emergency Physicians, and the Family Physicians Airways Group of Canada).

Main message Diagnosis of ABRS is based on the presence of specific symptoms and their duration; imaging or

EDITOR'S KEY POINTS

- Rhinosinusitis is a common malady, afflicting approximately 1 in 8 adults. Sinus symptoms are a common complaint among patients seeking medical attention, but up to two-thirds of patients with sinus symptoms have viral disease rather than bacterial infection. Antibiotics were once routinely prescribed on the suspicion of acute bacterial rhinosinusitis (ABRS), but treatment emphasis has shifted as antimicrobial resistance rates have increased.
- The Canadian guidelines for the diagnosis and management of ABRS provide up-todate recommendations to help clinicians diagnose and treat their patients with ABRS. Although lacking in specificity, using duration-based symptoms for the diagnosis of uncomplicated cases of ABRS is the best available approach for diagnosis in the office setting. Intranasal corticosteroids have emerged as modestly beneficial as adjunct therapy or as monotherapy, with antibiotics reserved for severe cases of disease in otherwise healthy adults.

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culture are not needed in uncomplicated cases. Treatment is dependent on symptom severity, with intranasal corticosteroids (INCSs) recommended as monotherapy for mild and moderate cases, although the benefit might be modest. Use of INCSs plus antibiotics is reserved for patients who fail to respond to INCSs after 72 hours, and for initial treatment of patients with severe symptoms. Antibiotic selection must account for the suspected pathogen, the risk of resistance, comorbid conditions, and local antimicrobial resistance trends. Adjunct therapies such as nasal saline irrigation are recommended. Failure to respond to treatment, recurrent episodes, and signs of complications should prompt referral to an otolaryngologist. The guidelines address situations unique to the Canadian health care environment, including actions to take during prolonged wait periods for specialist referral or imaging.

Conclusion The Canadian guidelines provide up-to-date recommendations for diagnosis and treatment of ABRS that reflect an evolving understanding of the disease. In addition, the guidelines offer useful tools to help clinicians discern viral from bacterial episodes, as well as optimally manage their patients with ABRS.

hinosinusitis is a common malady, afflicting approximately 1 in 8 adults. The incidence of acute rhinosinusitis among American adults rose from 11% (26 million) in 2007¹ to 13% (29.8 million) in 2010.2 Applying the more recent prevalence rate to the Canada population results in an estimated 3.5 million adults with acute rhinosinusitis annually.3

Sinus symptoms are a common complaint among patients seeking medical attention. However, up to two-thirds of patients with sinus symptoms have viral disease rather than bacterial infection.4 Although antibiotics were once routinely prescribed on the suspicion of acute bacterial rhinosinusitis (ABRS), treatment emphasis has shifted as antimicrobial resistance rates have increased. In 2011, Canadian clinical practice guidelines were published for ABRS and chronic rhinosinusitis (CRS)^{5,6} to address

the evolving state of diagnosis and treatment while addressing aspects unique to the Canadian health care system (eg, prolonged wait times for medical procedures and specialist referral7).

Quality of evidence

Guideline authors performed a systematic literature search and drafted recommendations. Recommendations received both strength of evidence and strength of recommendation ratings. Input from external content experts was sought, as was endorsement from Canadian medical societies (Association of Medical Microbiology and Infectious Disease Canada, Canadian Society of Allergy and Clinical Immunology, Canadian Society of Otolaryngology—Head and Neck Surgery, Canadian Association of Emergency Physicians, and the Family Physicians Airways Group of Canada). Ratings for the strength of the evidence and the strength of the recommendations (reflective of the expert panel's confidence) are provided in the full guideline. Among the 14 clinical experts involved in guideline development, 3 were family physician members of the Family Physician Airways Group of Canada. Funding for guideline development and review was provided through an unrestricted grant obtained from 5 pharmaceutical companies. No contact was made with the grantors during the guideline development and review process.

Main message

Pathophysiology. Acute bacterial rhinosinusitis is a disease of bacterial infection, and often involves a predisposing condition (Box 1)8 that initiates an inflammatory process in the nasal mucosa and sinuses. The inflammatory process leads to constriction of nasal passages, poor drainage of mucus from the sinuses, and poor tissue oxygenation, which predispose the area to microbial growth.

Multiple studies have identified Streptococcus pneumoniae and Haemophilus influenzae as the 2 main pathogens in ABRS, accounting for more than half of cases.9-13 Moraxella catarrhalis is a less common pathogen in adults, but accounts for a quarter of cases in children.14 Streptococcus pyogenes, Staphylococcus aureus, Gram-negative bacilli, and oral anaerobes are also less common pathogens in ABRS. 10,15,16 Peptostreptococcus spp, Fusobacterium spp, and Prevotella spp, as well as mixed anaerobic and facultative anaerobic bacteria (α-hemolytic streptococci, microaerophilic streptococci, and S aureus) are anaerobic organisms commonly associated with ABRS of odontogenic origin.17

Diagnosis. The guidelines propose a mnemonic device, PODS (facial Pain, pressure, or fullness; nasal Obstruction; nasal purulence or discoloured postnasal Discharge; and Smell disorder), to aid recall of the important symptoms to assist in diagnosis (Figure 1).5,6 Minor symptoms (cough, dental pain, ear pain or pressure, fatigue, halitosis, and headache) are considered supportive of a diagnosis.

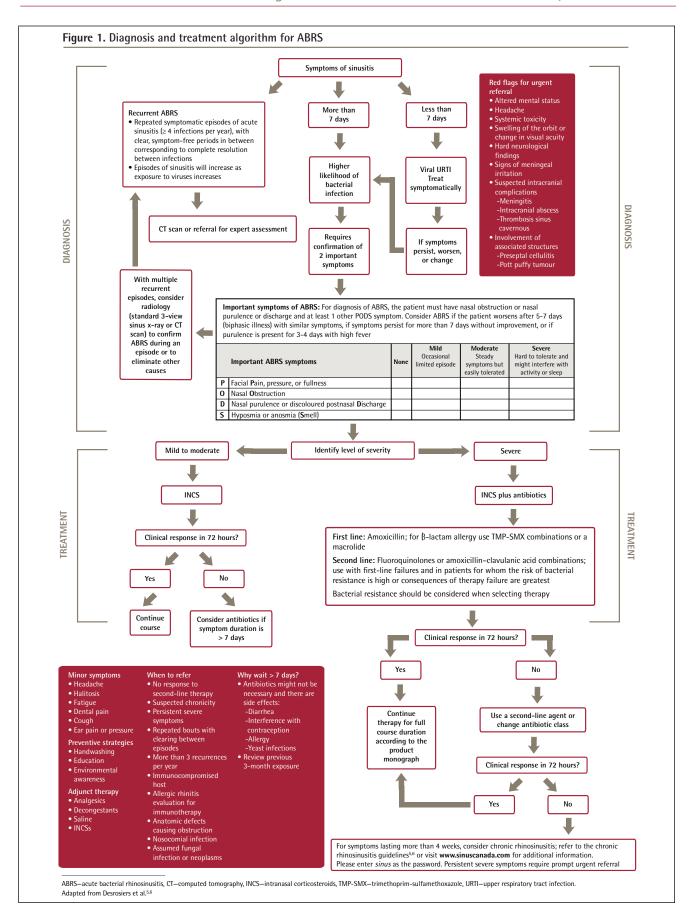
Prediction rules, while not diagnostic, can help bolster a diagnosis of ABRS. 4,18,19 The presence of 3 or more Berg criteria (purulent rhinorrhea with unilateral predominance, local pain with unilateral predominance, pus in the nasal cavity, or bilateral purulent rhinorrhea) has a positive likelihood ratio of 6.75 for ABRS, while the presence of 4 or more Williams criteria (maxillary toothache, poor response to antihistamines or decongestants, abnormal transillumination, purulent nasal secretions, and coloured nasal discharge) has a positive likelihood ratio of 6.4 for ABRS.

A diagnosis is both symptom specific and duration based, requiring the presence of at least 2 important symptoms (1 of which must be nasal obstruction, nasal purulence, or discoloured postnasal discharge) present for at least 7 days without improvement (Figure 1)5,6 or in a biphasic fever-illness pattern. Because common colds caused by rhinoviruses present with symptoms similar to ABRS, the duration of symptoms is important to help exclude viral cases. A common cold reaches peak symptom severity by 3 days and improvement is noted by 7 days. 10 Persistence or worsening of viral symptoms suggests a complication such as bronchitis, rhinosinusitis, or pharyngitis.20 Up to 2% of viral upper respiratory tract infections progress to ABRS.10

Acute bacterial rhinosinusitis is further characterized by a sudden onset of symptomatic sinus infection lasting less than 4 weeks. Symptoms completely resolve during this recovery period either spontaneously or with treatment.21,22 While ABRS is characterized by 3 or fewer episodes per year, 4 or more episodes is classified as recurrent ABRS.

Diagnosis in the primary care setting does not require routine nasal culture or other invasive procedures, unless there are complications or unusual evolution. For uncomplicated cases, diagnosis is made based on findings from a thorough history and physical examination (Box 1).8

Role of imaging. Although radiologic imaging is not necessary for diagnostic purposes in uncomplicated cases of ABRS, imaging might be beneficial for patients who present with recurrent ABRS or for patients whose symptoms necessitate ruling out other causes of disease. In such cases, imaging (3-view plain sinus x-ray or computed tomography [CT] scan) can provide critical additional information that might aid in diagnosis. Imaging results suggestive of ABRS include complete opacification of the image, or the presence of an air or fluid level. Mucosal thickening as a sole characteristic is not diagnostic for ABRS because this finding can be observed in asymptomatic patients23 and in most instances of viral



Box 1. Medical history and physical examination for ABRS

History

- Assess for predisposing conditions
- -Recent viral URTI
- -Allergic rhinitis
- -Nonallergic rhinitis
- -Rhinitis medicamentosa
- -Concomitant conditions (eg, pregnancy, immunodeficiency, hypothyroidism, cystic fibrosis, migraine, vascular headache)
- -Anatomic causes (eg, deviated septum, turbinate deformity, enlarged tonsils or adenoids, nasal polyps, nasal foreign body, tumour)
- Poor response to decongestant use
- Facial pain above or below the eye area, increasing pain with bending forward Physical examination
- Probe for tenderness by palpation and percussion of the
- Areas to palpate include
- -Maxillary floor from palate
- -Lateral ethmoid wall from medial angle of eye
- -Frontal floor from roof of orbit
- -Anterior maxillary wall from cheek
- -Anterior front wall from supraorbital skull
- Localizing the site of pain might implicate a specific sinus
- Tap maxillary teeth (use tongue depressor) for tenderness, indicating bacterial maxillary sinusitis
- Visualize purulent secretions in the middle meatus (can use a wide speculum mounted on an otoscope if a nasal speculum is unavailable)
- -A topical vasoconstrictive agent can assist in visualization
- Inspect posterior pharynx (use pharyngeal mirror) for purulent secretions

ABRS—acute bacterial rhinosinusitis, URTI—upper respiratory tract infection.

Data from Desrosiers.8

upper respiratory tract infections.²⁴ Imaging results should always be considered alongside clinical symptoms.

Red flags for urgent referral. Symptoms that indicate extension of disease from the sinuses to the orbit or intracranial structures (Figure 1)^{5,6} require urgent specialist referral and aggressive treatment.25-27 Symptoms include orbital pain, high fever, and edema (indicating preseptal cellulitis); limitation of ocular motion, pain, tenderness, conjunctival chemosis, exophthalmos (postseptal inflammation); fixated globe and diminished visual acuity (subperiosteal or orbital abscess); blindness (occlusion of central retinal artery, optic neuritis, corneal ulceration, panophthalmitis); and altered mental status with high fever, frontal or retro-orbital migraine, or the presence of generic signs of meningeal irritation (intracranial complications [eg, brain abscess, cavernous sinus thrombosis, meningitis]).

Treatment. The goal of therapy is to improve symptoms by controlling infection, reducing edema, and reversing sinus ostial obstruction.28 Guidelines recommend using disease severity to help direct therapy. Severity is based on the duration and intensity of symptoms, coupled with the effect of the disease on patient quality of life (Figure 1).5,6 For mild to moderate ABRS, intranasal corticosteroids (INCSs) can be used to meet treatment goals. By reducing inflammation, INCSs promote sinus drainage and improve sinus ventilation.²⁹ In a clinical study, mometasone furoate for 15 days significantly improved symptoms scores, beginning at day 2, compared with amoxicillin for 10 days (P=.002) or placebo (P<.001).30 Compared with placebo treatment, mometasone furoate was associated with significantly improved quality of life for patients with ABRS (P=.047).³¹ Of note, mometasone furoate is approved in Canada for the treatment of acute rhinosinusitis, with or without signs or symptoms of bacterial infection.³² Although the guideline recommendations were based on limited evidence, a new study adds further support for the use of INCS monotherapy.33 In this study, patients meeting entry criteria, including signs and symptoms of rhinosinusitis lasting 8 to 13 days, were randomized to fluticasone furoate nasal spray (110 µg once or twice daily) or placebo for 15 days.33 Mean daily, morning, and evening symptoms scores were statistically improved, but only moderately clinically improved (-2.97 for placebo, -3.36 for fluticasone once daily, and -3.33 for fluticasone twice daily) for the fluticasone-treated groups versus the placebo group. There was no significant benefit in time to symptom improvement or the validated SNOT-20 (Sino-Nasal Outcome Test) scores, but fluticasone furoate treatment was associated with significantly improved patient productivity and sleep versus placebo (P < .05).³³ The addition of antibiotic therapy was low across treatment arms (3%). Of the 4 studies of INCS monotherapy to date, only 1 study reported no benefit. However, this study used the lower potency INCS, budesonide, and enrolled patients with a symptom duration of as little as 4 days.34 The median days of symptom duration at presentation was shorter (7 days, with a range of 4 to 14 days) than currently recommended for treatment initiation. Treatment might not be necessary unless symptoms have persisted for at least 7 days. Overall, the lack of efficacy reported for INCSs and antibiotics in this study likely reflects that many cases were viral in nature.

The recommendation for INCS use is bolstered by the most recent study findings, and continues to be supported by other newly published guidelines.³⁵ Treatment with INCSs has not been associated with complications, increased adverse events, or recurrence.³⁶ The Infectious Diseases Society of America guidelines do make a weak recommendation to use INCSs primarily in patients with

a history of allergic rhinitis.³⁷ If there is no improvement in symptoms after 3 days of INCS monotherapy, addition of antibiotics should be considered

What about antibiotics? The efficacy of INCSs used with antibiotics was reported in a meta-analysis that found significant benefit of 15 to 21 days of INCS therapy (budesonide, fluticasone propionate, or mometasone furoate) added to antibiotic therapy in improving the symptoms of cough and nasal discharge in patients with ABRS.³⁶ In this meta-analysis, combination of all treatment arms resulted in 73% and 66% of patients in the treated and placebo groups, respectively, experiencing improvement by study end, yielding a number needed to treat of 15 and a relative risk reduction of 9%. 36,37 While numbers needed to treat from the individual studies range from 5 to 31, it should be noted that different patient populations, drug potencies, and drug concentrations were studied. In one of the studies, patients with moderate to severe ABRS who received amoxicillin-clavulanate plus mometasone furoate reported significantly improved symptom scores (days 1 to 15 averaged) versus patients taking antibiotic monotherapy $(P \le .017)$. ³⁸ In a study of patients with ABRS and history of recurrent sinusitis or chronic rhinitis, patients receiving cefuroxime axetil plus fluticasone propionate spray reported a significantly higher rate of clinical success (93.5% vs 73.9%, P=.009) and shorter duration of symptoms (6 days to clinical success vs 9.5 days, P<.01) compared with the antibiotic monotherapy group.³⁹ There were no significant adverse events with INCSs and no recurrence of disease. In an observational study of patients presenting to their primary care physicians with clinical symptoms of rhinosinusitis of at least 7 days' duration, treatment was assigned according to local practice standards. 40 The affect of 15 days of treatment on main symptom scores and quality of life was analyzed. Intranasal corticosteroids, antibiotics, and oral decongestants were prescribed to 91%, 61%, and 27% of patients, respectively. Main symptom scores improved from baseline to day 15 (from 8.4 to 1.9). At baseline, 88.4% and 43.2% of patients reported pain or discomfort and problems with usual activities, respectively, while 31.5% and 1.4% of patients reported these health issues on day 15. The study authors noted that 90% of patients demonstrated clinically relevant improvement. Guidelines recommend that antibiotics be reserved for the treatment of severe symptoms, for patients with underlying comorbid disease, those at risk of complications, or for patients concerned about quality of life or productivity. This approach supports efforts by the World Health Organization to promote rational antibiotic use. 41 Meta-analyses of antibiotic clinical trials for ABRS report decreased risk of clinical failure by as much as half with antibiotics. 42-44 However, these results

are tempered by the observation that a high percentage of placebo-treated patients also reported an improvement or resolution of symptoms at 7 to 14 days (69%42 to 80%⁴³). A recent study of patients with moderate to severe symptoms of ABRS, or with biphasic illness, adds to the literature questioning the utility of antibiotics in ABRS. 45 Amoxicillin and placebo groups reported similar improvements in symptoms and quality of life at days 3 and 10, while the amoxicillin group reported a small but statistically significant difference on day 7. Lack of efficacy was not attributed to antimicrobial resistance, which was low in this population. One meta-analysis reported faster symptom resolution and a lower rate of complications in antibiotic- versus placebo-treated patients, but similar rates of relapse.44 In addition, antibiotics are associated with an increased incidence of side effects, with one meta-analysis reporting nearly a 2-fold increase in rate of adverse events in the antibiotic group compared with the placebo group.44

When a decision to prescribe antibiotics is made, several factors weigh in antibiotic selection (Box 2). 22,46-48 First-line therapy consists of amoxicillin. A macrolide or trimethoprim-sulfamethoxazole (TMP-SMX) combination should be used for patients with β-lactam allergy. Secondline agents include amoxicillin-clavulanic acid combinations or fluoroquinolones with enhanced Gram-positive activity (Figure 1).5,6 Failure of response after 72 hours of

Box 2. Factors to consider when prescribing antibiotics

- Suspected pathogen
- Medical history can indicate that a second-line agent should be used for initial treatment
- -Underlying medical conditions that place patient at increased risk of complications if first-line treatment fails
- -Systemic disorders (eg, chronic renal failure, immune deficiency, diabetes) place patients at increased risk of complications, antibiotic resistance, and risk of recurrence
- -ABRS of the frontal or sphenoidal sinuses places patients at higher risk of developing complications than patients with maxillary and ethmoid sinusitis22
- -Chronic medical conditions or underlying immunosuppressive sites or medications
- Potential risk of resistance, based on
- -Previous 3-mo exposure to antibiotics (associated with pneumococcal resistance⁴⁶)
 - If yes, prescribe antibiotic from a different drug class⁴⁷
- -Exposure to day-care settings (associated with penicillinand macrolide-resistant streptococci⁴⁸)
- -Chronic symptoms (ie, longer than 4 wk)
- Local patterns of antimicrobial resistance
- -High resistance rates to penicillin and macrolide antibiotics
- -Recognize regional variability in patterns of resistance
- Antibiotic tolerability, cost, convenience

ABRS-acute bacterial rhinosinusitis.

antibiotic treatment indicates antibiotic resistance and the antibiotic should be changed to another class or a secondline agent. When antibiotics are used, a 10-day course is considered sufficient. Improvement in symptoms despite their incomplete disappearance is not cause for immediate use of a second antibiotic. Current costs of antibiotic and INCS treatment are presented in Table 1.49,50

Antimicrobial resistance. Because antimicrobial resistance substantially affects health care costs, medical outcomes, and options to control infectious disease, 51,52 care is needed when selecting antibiotics. In Canada, the rate of penicillin nonsusceptibility of S pneumoniae isolates reached 17% in 2007,53 after hovering near 15% since 1998.54 The highest resistance rate is for erythromycin (19%), which presents some concern

Table 1. Cost of medications for acute bacterial rhinosinusitis

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MEDICATION	COST, \$
Antibiotics (10-d course unless otherwise specified)	
 Amoxicillin, 500 mg 3 times daily* 	11.03
 Azithromycin for 5 d (500 mg on first day, 250 mg for 4 d)* 	11.57
 Amoxicillin-clavulanate, 500 mg 3 times daily or 875 mg twice daily* 	20.00
 Clarithromycin extended-release formulation, 2 times 500 mg daily* 	50.03
 Cefprozil, 250-500 mg twice daily* 	8.60-11.70
 Cefuroxime axetil, 250-500 mg twice daily* 	14.50-28.70
 Doxycycline, 100 mg twice on the first day, then 100 mg daily* 	5.90
 Levofloxacin, 500 mg daily* 	13.37
 Moxifloxacin, 400 mg daily* 	58.20
 Trimethoprim-sulfamethoxazole, 1 or 2 double-strength doses twice daily* 	0.8-2.40
 Azithromycin sustained-release, 2-g single dose 	31.37 (Ontario cost to wholesaler†)
Nasal steroids: 1 inhaler (2 wk of therapy at 2 puffs twice daily)	
 Fluticasone furoate, 110 mg, 2 puffs twice daily times 1 inhaler[†] 	24.76
 Mometasone furoate, 50 μg, 2 puffs twice daily times 1 inhaler[§] 	28.91

^{*}Data from Medication Use Management Services.49

for potential cross resistance to other macrolides (eg, azithromycin, clarithromycin). Amoxicillin has retained activity against S pneumoniae (<2% resistance).55,56 Resistance rates to fluoroguinolones (ie, ciprofloxacin, levofloxacin, moxifloxacin, gatifloxacin) also remain low (<2.5% in 2005).54

The increasing incidence of β-lactamase-producing strains of H influenzae and M catarrhalis, which results in ampicillin resistance, is a growing concern. Across Canada, 19% and 92% of H influenzae and *M catarrhalis* isolates, respectively, were found to produce β-lactamase. 57 Resistance rates to β-lactamaseproducing H influenzae were low for amoxicillin-clavulanate (0.2%), the cephalosporins (0.5% to 12.2%), the fluoroquinolones (0% to 0.1%), and clarithromycin (1.9%), while resistence to TMP-SMX (18.5%) was higher. 57

Despite its propensity to produce β-lactamase, M catarrhalis remains susceptible to nearly all antibiotics except for the amino-penicillins.⁵⁷ In the United States, 4% of ABRS cases were associated with community-acquired, methicillin-resistant S aureus,58 which is usually susceptible to clindamycin, doxycycline, and TMP-SMX, but resistant to β-lactam antimicrobials.59

Controversies in antibiotic use. It should be noted that recommendations for antibiotic use and choice differ in other recently published guidelines (ie, the Infectious Diseases Society of America guidelines for ABRS in children and adults³⁷ and the Medication Use Management Services guidelines for community-acquired infections⁴⁹). Canadian guidelines reserve antibiotics for specific cases of ABRS and are consistent with previous international guidelines^{60,61} and other recent guidelines³⁵ for treating ABRS. Differences in antibiotic choice partly reflect the differing resistance patterns considered by the authoring groups. Specific antimicrobial agents not mentioned in the Canadian guidelines might also be appropriate. Indeed, antibiotic agent recommendations are likely to change with the evolving landscape of antimicrobial resistance rates. Ultimately, clinical judgment and local resistance patterns are paramount when selecting antibiotics.

Adjunct therapy. Although clinical trial evidence is sparse for adjunct therapies in the treatment of ABRS, these therapies might help alleviate symptoms associated with ABRS. Analgesics (eg, nonsteroidal antiinflammatory drugs, acetaminophen), oral and topical decongestants, and nasal saline irrigation have been reported to help alleviate symptoms. Topical decongestants are controversial and should not be used for longer than 3 days owing to the risk of rebound congestion. Studies of oral decongestants for the treatment of ABRS in adults are lacking; however, Canadian and other guidelines recommend oral decongestants as an option for patients without contraindications

[†]Data from personal communication with Pfizer Canada.

[†]Data from personal communication with GlaxoSmithKline Canada. Note this product does not have an acute sinusitis indication at this

[§]Data from IMS Brogan DeltaPA wholesaler prices database.50

owing to the efficacy of such agents in improving nasal congestion. Although patients with a strong allergy component might benefit from adjunct antihistamine use, this medication is not recommended for nonatopic adults with ABRS because of the risk of exacerbating the episode by drying nasal mucosa.61

Follow-up. Lack of a response to treatment within 72 hours requires progression to the next level of therapy (Figure 1).5,6 If failure occurs after a second course of antibiotic therapy, specialist assessment is warranted. When specialist or CT wait times are long (≥6 weeks), a CT should be ordered and empiric therapy for CRS should be initiated during the wait period.5

For patients with clearing of uncomplicated ABRS and early recurrence, a trial of INCSs should be considered, as well as specialist referral. Possible contributions from allergy and immunologic factors should also be evaluated. Urgent referral should be provided for patients with persistent or recurrent episodes with severe symptoms. Patients with recurrent ABRS or treatment failure after extended courses of antibiotics likely have CRS, and specialist referral will provide the objective finding (endoscopy or CT) necessary for diagnosis. Further indications for referral are listed in Figure 1 (lower left box).5,6

Conclusion

The Canadian guidelines for the diagnosis and management of ABRS provide up-to-date recommendations to help clinicians correctly diagnose and treat their patients with ABRS. Although lacking in specificity, using duration-based symptoms for the diagnosis of uncomplicated cases of ABRS is the best available approach for diagnosis in the office setting. Intranasal corticosteroids have emerged as modestly beneficial as adjunct therapy or as monotherapy, with antibiotics reserved for severe cases of disease in otherwise healthy adults. Direction for managing patients while awaiting medical procedures or specialist assessment is provided. The Canadian guidelines for ABRS provide helpful tools to assist clinicians in effectively diagnosing and managing their patients with this disease.

Dr Kaplan is a family physician practising in Richmond Hill, Ont, a staff physician at Brampton Civic Hospital, and Chair of both the Family Physician Airways Group of Canada and the Respiratory Medicine Program Committee of the College of Family Physicians of Canada.

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Competing interests

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